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Review Article

Beta-Endorphins: Anti-inflammatory Activity in Holistic Treatment of Diseases

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Abstract

Endorphins are an endogenous morphine, neuropeptide, produced from pituitary gland in response to stress and pain. These are of three types beta-endorphins, enkephalins, dynorphins binds to mu, kappa, delta receptors found on immune cells and nervous system. Beta-endorphins are an abundant endorphin synthesized and stored in the anterior pituitary gland. It has got various activities such as immune stimulatory, anti-inflammatory, analgesic, anti-ageing, stress buster activity involved in preventive, promotive, therapeutic and palliative treatment of various diseases such as cancer, chronic inflammatory diseases such as heart disease, Alzheimer's disease, diabetes mellitus, auto-immune disease, and infectious disease without any adverse effects. Endorphins especially beta-endorphins used in treatment of many diseases by its anti-inflammatory activity where chronic inflammation is considered as the basis for most of all diseases. This article highlights about the basic original research findings regarding anti-inflammatory role of beta-endorphins in treatment of various diseases.

Keywords: *Chronic Psychological Stress; Cortisol; Noradrenaline; ACTH; NF-KB; STAT-3; IL-1; IL-6; TNF-α; COX-2*

Abbreviations

PNS: Peripheral Nervous System; CNS: Central Nervous System; ACTH: Adrenocorticotropic Hormone; HPA- Axis: Hypothalamic Pituitary Adrenal Axis; STAT 3: Signal Transducer and Activator of Transcription Protein 3; NF-kB: Nuclear Factor Kappa- Light- Chain-Enhancer of Activated B Cells; CRH: Corticotropin Releasing Hormone; COX-2: Cyclooxygenase 2; TNF- α: Tumor Necrosis Factor - Alfa; IFN- γ: Interferon Gamma

Introduction

Holistic healing is a whole person healing. Human body works as a whole. If we consider human body as a whole rather than as parts in treating any diseases with reductionist chemical drugs yields better results without adverse effects. Human body has an excellent capacity to combat against many diseases. Adverse drug reaction is a major killer in the present world. Endorphins are endogenous morphine, neuropeptides produced in pituitary gland response to stress and pain. There are three types of endorphins beta-endorphins, enkephalins, and dynorphins binds to μ(mu) , k(kappa) , and δ(delta) receptors situated on nervous system and immune cells.

Beta-endorphins is an abundant endorphin, potent than morphine, synthesized and stored in the anterior pituitary gland, it is a precursor of POMC (Proopiomelanocortin) [1-6].

Mechanism of action of beta-endorphins

Most of all immune cells produce endorphins. In inflammatory state recruitment of immune cells to the site of inflammation by chemokines produce endorphins reduce inflammation by binding of endorphins to the receptors on peripheral nerves results in inhibition of substance p a neurotransmitter of pain and inflammation, produce of IL-18, IL-10, and IFN-γ anti-inflammatory cytokines [22,23,26,27].

Endorphins produced during pranic healing yoga, Love, tender, care, intense physical exercise creates a psychological relaxed state known as "Runner's high", meditation, pranayama, music therapy, acupuncture, sympathy, empathy in caring for the patient [6-10,13-15,18,19].

Chronic psychological stress induced release of CRH (corticotrophin releasing hormone) from hypothalamus activates HPA-axis through ANS (Autonomic nervous system) release neuropeptides such as cortisol, noradrenaline, and ACTH activates IL-1β, TNF-α, IL-6 and COX-2, inflammatory mediators, which activates NF-KB, STAT-3 transcription factors involved in chronic inflammatory diseases (heart diseases and Alzheimer's disease), autoimmunity, diabetes mellitus, infectious disease, and cancer [22-28].

In the peripheral nervous system (PNS) binding of beta- endorphins to the μ (mu) receptors on peripheral nerves results in inhibition of substance P a neurotransmitter of pain and inflammation. In the central nervous system (CNS) binding of beta-endorphins to the μ (mu) receptors on central nervous system instead of inhibiting substance p, it inhibits GABA (Gama amino butyric acid) inhibitory neurotransmitter, activates dopamine neurotransmitter involved in analgesic activity, euphoria, tranquillity of mind, self-reward, cognitive development and stress buster activity [17,22,23,26-30].

Endorphin receptors are situated on most of all immune cells. Binding of beta endorphins to the μ (mu) receptors on innate and adaptive immune cells such as NK cells, DC's, neutrophils, macrophages, T cells, and Bells results in activation of immune cells (immunestimulatory activity), release of opsonin, granzyme-B, IFN-Ƴ and antibodies involved in antiviral activity, antibacterial activity, antifungal activity, antitumor activity, and anti-inflammatory activity [9-12,14-16].

Beta endorphins inhibits chronic psychological stress induced sympathetic nervous system activity and activates parasympathetic nervous system activity mediated inhibition of release of neuropeptides such as cortisol, ACTH, noradrenaline, through inhibiting HPA-axis results in inhibition of inflammatory mediators release such as IL-1β, TNF-α,IL-6 and COX-2, which activates NF-KB, STAT-3 transcription factors involved in chronic inflammatory diseases (heart diseases, Alzheimer's disease), autoimmunity, diabetes mellitus and cancer [20,22,23,26-28,31].

Beta endorphins inhibits key transcription factor NF-KB transcription factor involved in tumor progression, which antagonize the P53 tumor suppressor gene, a guardian of the genome mutated in more than 50% of all cancers by inflammatory mediators such as NO (Nitric oxide), ROS (Reactive oxygen species), RNS (Reactive nitrogen species), Activation induced cytidine deaminase (AID) enzyme [22,23,26-28].

Beta endorphins express epithelial E-Cadherin involved in epithelial attachment, loss of E- cadherin involved in EMT (epithelial mesenchymal transition) induced tumor invasion.

Beta endorphins reduces chronic psychological stress by reducing noradrenaline neuropeptide secreted during chronic psychological stress through inhibition of HPA-axis mediated by ANS (Autonomic nervous system), which is responsible for releasing glucose from the liver increases blood glucose level in patients with non-insulin dependent diabetes mellitus.

Beta endorphins delay aging by lengthening telomeres, which otherwise shorten with aging and other mechanism is by inhibiting free radicals (ROS,RNS) release during oxidative stress via NADPH oxidase pathway produced by inflammatory cells such as neutrophils, macrophages, and dendritic cells involved in cell aging, genetic mutation, tissue damage, DNA damage and cell death.

Beta endorphins inhibits chronic psychological stress induced NF-KB a key transcription factor induced expression of inflammatory mediators such as chemokines, cytokines, growth factors, and proteolytic enzymes involved in conversion ofTH1 lymphocytic type to TH2 lymphocytic type produce IL-4, IL-13, IL-5 pro-inflammatory cytokines, and TH17 cells facilitate chronic inflammation, immune modulation, and tissue damage. Altered induced Tregs (Regulatory T cells) formed from TH1 mediated by cells TGF-β inflammatory mediator release IL-4, IL-5, IL-10, IL-13, IL-2, IL-17 proinflammatory cytokines involved in immune modulation otherwise normally involved in self-tolerance and immune homeostasis. Growth factors such as (EGF, FGF, VEGF) involved in cell proliferation and angiogenesis, proteolytic enzymes such as mmp's (matrix metalloproteases) involved in tissue damage, all these changes leads to autoimmune disease [23-27].

Endorphins are endogenous morphine acts as natural a holistic preventive, therapeutic, promotive, and palliative treatment of diseases such as autoimmune diseases, cancer, and infectious diseases without adverse effects and inexpensive. Thorough understanding of endorphins, activities that produce endorphins, mechanism of action, dose dependent duration of action, prognosis related to disease helpful for future therapeutic applications in diseases.

Conclusion and Future Perspective

Endorphins are neuropeptides produced from pituitary gland in response to pain and stress. Chronic psychological stress release CRH from hypothalamus activate HPA-Axis through ANS release noradrenaline neuropeptides such as cortisol, ACTH and nor-epinephrine mediated activation of inflammatory mediators IL-1ß, TNF-α, IL-6, and COX-2 from inflammatory cells activate NF-KB, STAT-3, transcription factors involved in tumor progression, auto-immune disease and infectious diseases. Beta-endorphins synthesize and stored in the anterior pituitary gland involved in immune stimulatory, anti-inflammatory, stress buster activity and analgesic activity. Chronic inflammation is a basis for most of all diseases. Because, of anti-inflammatory activity of beta-endorphins used to treat diseases such as cancer, auto-immune diseases, infectious diseases and chronic inflammatory diseases such as heart diseases and Alzheimer's disease without adverse effects and inexpensive.

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